EXHIBIT 1

MASTER SERVICES AGREEMENT

THIS MASTER SERVICES AGREEMENT ("Agreement") is entered into as of the 19th day of March 2018 ("Effective Date") by and between **Regulatory & Clinical Research Institute, Inc.**, with its office located at 5353 Wayzata Boulevard, Suite 505, Minneapolis, MN 55416-1334, USA ("RCRI") and **Physeon GmbH,** with a place of business at Herrenacker 15, 8200 Schaffhausen, Switzerland ("Company"). In this Agreement, Company and RCRI may be referred to individually as a "Party" and collectively as the "Parties".

Recitals

A. RCRI provides various consulting services to medical product manufacturers, including assistance with submissions to domestic and overseas regulatory agencies, regulatory compliance, clinical trial design, management and analysis of data from clinical studies, preclinical study design, quality systems and compliance, health economics and outcomes research, and continuing education and training.

B. Company, a medical product manufacturer, has a need for various consulting Services (as defined below) and desires to retain RCRI to provide such Services, and RCRI desires to be engaged by Company to provide such Services, all subject to the terms and conditions of this Agreement and any applicable Work Order(s) (as defined below).

NOW THEREFORE, in consideration of the foregoing and the mutual covenants, agreements, representations and warranties contained herein, the Parties hereto agree as follows:

Agreement

1. Scope of Work.

1.1 RCRI agrees to provide to Company the consulting services set forth in detailed work orders ("Work Orders") executed by RCRI and Company ("Services") using the format, or a format substantially similar to the format, attached as Schedule 1.

1.2 Each Work Order hereunder shall refer to and be part of this Agreement and shall be governed by the terms and provisions hereof, in addition to the specific details set forth in the Work Order. To the extent any terms or provisions of a Work Order conflict with the terms and provisions of this Agreement, the terms and conditions of this Agreement shall control, except to the extent that the applicable Work Order expressly and specifically states an intent to supersede the Agreement on a specific matter.

1.3 Except for the Services described in Work Orders that are accepted by both RCRI and Company, Company is under no obligation to retain RCRI to provide any services, nor is RCRI under any obligation to provide services to Company.

2. Company Information.

Subject to Section 5.5 below, Company agrees to provide to RCRI all necessary information regarding Company's applicable medical product ("Company Information") as is deemed necessary by RCRI to perform the Services, in a timely manner and in any format which may be reasonably specified by RCRI. Company acknowledges that Company, whether directly or through its designated third parties, is the only source for Company Information and that RCRI shall not be responsible for independently verifying the accuracy or completeness of Company Information.

3. Fees and Payment.

3.1 Fees. Unless otherwise agreed upon in a Work Order, Company shall pay RCRI's hourly fees set forth in RCRI's applicable fee schedule ("Fee Schedule"). The current Fee Schedule is attached as Exhibit A. RCRI reserves the right to modify the Fee Schedule as necessary or on an annual basis upon providing at least thirty (30) days advance notice. RCRI also reserves the right to modify the Fee Schedule in the event of extraordinary requests, including but not limited to the placement of RCRI personnel on-site at Company locations, or deadlines for which substantial overtime will be involved. RCRI's hourly rates for Services of an extraordinary nature shall be set forth in an applicable Work Order. Fees will be invoiced based on: (1) the hourly rates in force for the calendar month during which Services are provided, and (2) the hourly rate for the respective staff member's job title during the month which Services are provided. Company shall also reimburse RCRI for all expenses incurred by RCRI as a result of performing the Services in accordance with Exhibit A. Unless otherwise agreed upon in a Work Order, RCRI will invoice Company, at least monthly, in arrears, for Services performed and expenses incurred as a result of performing Services.

3.2 Payment. The fees and/or expenses invoiced by RCRI shall be payable by Company within thirty (30) days of the date of receipt of the respective invoice. RCRI reserves the right to charge a finance charge on all undisputed overdue amounts at the rate of 9% APR. If any undisputed amounts remain outstanding for more than thirty (30) days after the invoice date, RCRI may immediately suspend the Services until the amounts are paid.

If Company disputes, in good faith, a charge on any invoice, it shall provide detailed written notice of its dispute with RCRI in regard to such portions of such invoice within ten (10) days of the date of receipt of the invoice ("Dispute Notification Period"). RCRI and Company will use all reasonable efforts to resolve and settle such dispute within thirty (30) days ("Dispute Resolution Period") following the Dispute Notification Period. However, all undisputed portions of invoices will be paid in accordance with this Agreement. If a resolution is not achieved by the Parties at the end of the Dispute Resolution Period, RCRI may immediately suspend the Services until the amounts are paid or terminate this Agreement. RCRI reserves the right to charge a finance charge on all disputed amount outstanding beyond the Dispute Resolution Period at the rate of 9% APR.

All amounts payable under this Agreement are exclusive of all sales, use, value-added, withholding, and other taxes and duties. Company will pay all taxes and duties assessed in connection with this Agreement by any authority within or outside of the U.S., except for

taxes payable on RCRI's net income. In the event that Company requests credit terms from RCRI, Company agrees to provide financial information to RCRI, as requested, to assess Company's creditworthiness.

4. Retainer.

Upon execution of a Work Order, Company shall pay the retainer amount specified on such Work Order. Notwithstanding anything to the contrary in this Agreement, the retainer shall be payable by Company upon signature of the Work Order by the Company. RCRI shall not perform any Services prior to receipt of the retainer. RCRI will hold this retainer until completion of the Services or termination of the applicable Work Order and will apply it, at Company's sole option, to the final invoice under the applicable Work Order or the retainer under the next Work Order. Unless otherwise specified by Company, RCRI will return any remaining balance no later than sixty (60) days after termination or expiration of this Agreement.

5. Confidential Information.

5.1 Definition. "Confidential Information" means all the information of any kind disclosed by one Party or its agents ("Disclosing Party") to the other Party or its agents ("Receiving Party") during the term of this Agreement that by its nature should reasonably be considered to be confidential or proprietary information.

5.2 Exceptions. Information will not be deemed Confidential Information hereunder if such information, as shown by documentary evidence (i) was known to the Receiving Party prior to receipt from the Disclosing Party directly or indirectly from a source other than one having an obligation of confidentiality to the Disclosing Party; (ii) becomes known (independently of disclosure by the Disclosing Party) to the Receiving Party directly or indirectly from a source other than one having an obligation of confidentiality to the Disclosing Party; (iii) was or becomes known or available to the public or otherwise ceases to be confidential or proprietary, except through a breach of this Agreement by the Receiving Party; or (iv) is independently developed by the Receiving Party without use of the Disclosing Party's Confidential Information.

5.3 Nondisclosure and Use of Confidential Information. With regard to Confidential Information received from the other Party, each Party agrees that it will use or allow such information to be used only in a manner consistent with the terms and purposes of this Agreement, and will maintain and preserve the confidentiality of such Confidential Information, including, without limitation, taking such steps to preserve and protect the confidentiality of the Confidential Information as it takes to preserve and protect the confidentiality of its own similar confidential information, but in no case less than reasonable precautions for the type of information disclosed. The Receiving Party may disclose the Disclosing Party's Confidential Information only to the Receiving Party's affiliated companies and its and their respective employees, accountants, attorneys and subcontractors who (i) have a need to know such Confidential Information, (ii) are made aware of the Confidential Information's confidential and/or proprietary nature and (iii) are under an obligation to protect confidential and/or proprietary information. Each Party will immediately notify the other Party if it is aware of any unauthorized use or disclosure of any Confidential Information by that Party, its

employees or agents, or any other entity. A Receiving Party may disclose Confidential Information if required by law or regulation, so long as such Party takes reasonable steps to provide prior notice to the Disclosing Party unless such prior notice is prohibited by law. Notwithstanding anything to the contrary in this Section 5, RCRI may disclose the identity of Company and the existence of this Agreement without obtaining prior approval from Company during any regulatory agency audit provided such agency has statutory authority over any work performed under the auspices of this Agreement.

5.4 Return of Confidential Information. Upon the written request of either Party or, at the option of the Receiving Party, 10 (ten) years after termination or expiration of the applicable Work Order, the Receiving Party may destroy, or, at the option and sole expense of the Disclosing Party, return to the Disclosing Party all tangible expressions of Confidential Information of the Disclosing Party (including all copies and all analyses, comparisons, studies or other documents prepared by the Receiving Party) unless the Disclosing Party requests the Receiving Party, in writing and at the Disclosing Party's expense, to return any tangible expressions of Confidential Information. Notwithstanding the foregoing, either Party may retain copies, including backups performed in accordance with the Receiving Party's standard operating procedures for data protection, of the other's Confidential Information solely for the limited purpose of its record-keeping, enforcing its rights under this Agreement before a court of competent jurisdiction or pursuant to the requirements of a governmental agency or by operation of law.

5.5 Privacy Laws. In accordance with all laws and regulations of the country of origin where the data originated, Company will remove from all information and data sent to RCRI, and will otherwise not transmit, provide, or make available to RCRI, any personal data, sensitive personal data, or individually identifying information regarding study subjects, including but not limited to an individual's name, address, email, telephone, number, government identification number, employee or workplace identification number, or similar information, unless the parties specifically agree, in an executed agreement, that Company Information will include such personal data, sensitive personal data, or individually identifying information.

6. License and proprietary Rights.

6.1 Company Information Rights. Solely for the purpose of performing the Services, Company grants to RCRI permission to use the Company Information. Nothing contained in this Agreement shall transfer ownership of any Company Information and data generated by RCRI from Company Information or limit in any way Company's ownership or right to use such data for any purpose.

6.2 Company's Proprietary Rights. Company will retain and have full ownership rights in all Company's products, materials, information, reports and other proprietary or protectable property that relate to Company's products and their applications and that are based on Company's Confidential Information, and that are developed or invented by RCRI in the course of providing the Services hereunder (collectively, "Company's Inventions"). All Company's Inventions and all deliverables will be the sole and exclusive property of Company and shall be Company Confidential Information. RCRI hereby assigns and transfers to Company all of RCRI's right, title and interest in any and all Company's

Inventions, agrees to take, at Company's request and expense, all further acts reasonably required to convey full title in the Company's Inventions to Company, and hereby waives any and all moral rights in any and all Company's Inventions. Solely for the purpose of performing the Services, Company grants to RCRI permission to use the Company's Inventions.

6.3 RCRI's Proprietary Rights. Company acknowledges that RCRI possesses certain inventions, processes, know-how, trade secrets, improvements, other intellectual property and other assets including but not limited to analytical methods, procedure and techniques, procedure manuals, personnel data, financial information; computer technical expertise and software, regulatory strategies, clinical strategies, quality strategies, standard operating procedures, work instructions, and templates which have been independently developed by RCRI and which relate to its business or operations (collectively "RCRI's Property"). All RCRI's Property is the sole and exclusive property of RCRI. Nothing in this Agreement shall transfer ownership of RCRI's Property or any improvements thereto or limit in any way RCRI's ownership or right to make commercial use of any derivatives of its intellectual property it creates, employs, improves, modifies, develops and/or produces in connection with providing its services under this Agreement, in which RCRI shall retain all rights, title, and interests.

7. Term and Termination.

7.1 Term. The term of this Agreement shall commence on the Effective Date and unless modified by mutual agreement of the Parties or terminated earlier pursuant to the terms herein, shall continue for a period of twelve (12) months thereafter. This Agreement shall automatically extend for additional twelve (12) month terms unless notice of termination is provided in writing by one Party to the other at least fourteen (14) days prior to the termination date. A Work Order shall commence on the date set forth therein and continue until terminated as set forth in this Agreement or the applicable Work Order.

7.2 Termination. Either Party may terminate this Agreement or any individual Work Order, with or without cause, by providing fourteen (14) days written notice to the other Party. Either Party may terminate this Agreement and/or any individual Work Order(s) immediately (i) for a material breach of this Agreement or the applicable Work Order(s) by the other Party, or (ii) where permitted by applicable law, if the other Party suffers a meeting of its creditors, has an administrator or receiver appointed in respect to any of its assets, or has a petition presented to appoint any such administrator or receiver.

7.3 Effect of Termination. The termination of this Agreement by either Party shall automatically terminate all Work Order(s), unless otherwise agreed upon by both Parties in writing. Upon termination of this Agreement for any reason (i) RCRI will cease providing Services; (ii) all accrued but unpaid fees and expenses through the date of termination will become immediately due and payable to RCRI; and (iii) the provisions in paragraphs 3, 4, 5, 6, 8, 9, 10, and 11 herein shall survive.

8. Indemnification.

8.1 By Company. Company will indemnify, defend and hold harmless RCRI and its directors, officers, shareholders, employees, representatives and assigns (each, an "RCRI Indemnified

Party"), from and against any and all losses, damages, judgments, settlements, liabilities, reasonable attorney fees, court costs, and expenses (collectively "Losses") resulting or arising from any third-party claims, suits, actions, proceedings, investigations or litigation relating to or arising from or in connection with this Agreement or the Services contemplated herein (including, without limitation, any Losses arising from or in connection with any study, test, device, product or potential product to which this Agreement relates), except to the extent such Losses are caused by a breach of this Agreement by RCRI, or the negligent acts, negligent omissions or intentional misconduct of the RCRI Indemnified Party.

8.2 By RCRI. RCRI will indemnify, defend and hold harmless Company and its directors, officers, shareholders, employees, representatives and assigns (each, a "Company Indemnified Party"), from and against any and all Losses resulting or arising from any third-party claims, suits, actions, proceedings, investigations or litigation relating to or arising from or in connection with this Agreement, any Work Order, or the Services contemplated herein, to the extent such Losses are caused by the breach of this Agreement by RCRI, or the negligent acts, negligent omissions or intentional misconduct of the RCRI Indemnified Party.

8.3 Notice. Each Party's indemnification obligations hereunder will be subject to (i) the indemnifying Party (a) receiving prompt written notice of the existence of any action; (b) at its option, controlling the defense of such action; and (c) receiving full cooperation of the indemnified Party in the defense thereof; and (ii) the indemnified Party not settling any Losses without the prior written consent of the indemnifying Party.

9. Warranties.

9.1 By RCRI. RCRI warrants that: (i) it has the right to enter into this Agreement; (ii) it will perform the Services in a professional and workmanlike manner and in accordance with all applicable laws and regulations; and (iii) it will make all reasonable efforts to provide adequate staff to complete the Services specified in the Work Order within the time frames set forth in the Work Order, if any, for those items for which it has sole authority. Company acknowledges that approvals and clearances of regulatory agencies are subjective and that RCRI does not give any warranty as to results, approval, or success of any submissions or the like to regulatory agencies. RCRI MAKES NO WARRANTY THAT THE SERVICES WILL BE ERROR-FREE. EXCEPT AS EXPRESSLY PROVIDED IN THIS SECTION 9.1, RCRI EXPRESSLY DISCLAIMS, AND COMPANY EXPRESSLY WAIVES, ANY AND ALL OTHER WARRANTIES, EXPRESS OR IMPLIED, REGARDING THE SERVICES OR ANY RESULTS, INCLUDING WITHOUT LIMITATION, THE IMPLIED WARRANTIES OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE, ANY WARRANTIES WITH RESPECT TO THE QUALITY, CONTENT, CONDITION OR USE OF RESULTS, AND ANY WARRANTY AGAINST INTELLECTUAL PROPERTY INFRINGEMENT OR THE LIKE.

9.2 By Company. Company warrants and represents that (i) it has the right to enter into this Agreement; (ii) it will perform all of its obligations hereunder and in accordance with all applicable laws and regulations; (iii) if applicable, Company will comply with all obligations imposed upon it as the sponsor of a clinical trial under applicable FDA laws regulations, including the registration obligations set forth in section 402 of the Public Health Service Act (42 U.S.C. 282); (iv) Company is authorized to use and transfer to RCRI all Company

Information; and (v) it shall provide all Company Information in compliance with all applicable laws and regulations, including but not limited to, HIPAA or the privacy laws of the country of origin of the clinical data (if applicable).

10. LIMITATION OF LIABILITY

EXCEPT FOR LIABILITY ARISING UNDER THIRD PARTY ACTIONS UNDER SECTION 8 ABOVE: (i) A PARTY'S LIABILITY TO THE OTHER PARTY UNDER THIS AGREEMENT WILL BE LIMITED TO DIRECT DAMAGES; AND (ii) NEITHER PARTY WILL BE LIABLE TO THE OTHER PARTY FOR ANY INCIDENTAL, CONSEQUENTIAL, INDIRECT OR PUNITIVE DAMAGES (INCLUDING WITHOUT LIMITATION, LOST PROFITS OR REVENUE, GOVERNMENT FINES OR ASSESSMENT, LOSS OF DATA, TECHNOLOGY, RIGHTS OR SERVICES, OR INTERRUPTION OF BUSINESS), EVEN IF ADVISED OF THE POSSIBILITY OF SUCH DAMAGES, WHETHER ARISING UNDER THEORIES OF CONTRACT, TORT, OR ANY OTHER THEORY OF LIABILITY, INCLUDING NEGLIGENCE. IN NO EVENT WILL RCRI'S LIABILITY UNDER THIS AGREEMENT EXCEED THE FEES PAID OR OWED BY COMPANY TO RCRI UNDER THE WORK ORDER THAT GAVE RISE TO THE CLAIM. IT IS AGREED THAT THE LIMITATIONS OF LIABILITY IN THIS SECTION 10 ARE AN ESSENTIAL BASIS OF THIS AGREEMENT.

11. Non-Solicitation and Conversion Fee.

11.1 Non-Solicitation. The Parties agree that during the term of this Agreement and for one (1) year after expiration or termination of this Agreement, neither Party shall directly solicit for employment in any capacity, any person who on the date hereof or at any time during the term of this Agreement is or becomes an employee of the other Party; provided that it will not be a violation of this Section 11.1 if an employee of a Party responds to an indirect solicitation (e.g. advertisements in media of general circulation).

11.2 Conversion Fee. If either Party violates Section 11.1 of this Agreement, it shall pay the other Party a contract conversion fee with respect to any employee who accepted employment with the breaching Party during the term of this Agreement or within one (1) year after expiration or termination of this Agreement. Such fee shall be equal to seventy-five percent (75%) of such employee's (1) ending annualized base salary with the non-breaching Party and (2) total bonus pay for the 12 month period immediately preceding employee's last day of employment with the non-breaching Party (excluding employee benefits, commissions, expenses, stock options or any other compensation). Such fee shall be paid in full by the breaching Party to the non-breaching Party within thirty (30) calendar days of the employee's first day of employment with the breaching Party. The conversion fee shall be in addition to any other remedies available to either Party by law.

12. General Terms.

12.1 Independent Contractors. RCRI and Company are independent contractors of each other. Nothing contained herein shall constitute an employment, partnership or joint venture relationship between the Parties. RCRI may use third parties under contract with RCRI to

assist RCRI in the performance of its obligations under this Agreement, provided that RCRI will remain responsible for all its obligations under this Agreement.

12.2 Assignments and Change in Control. This Agreement shall inure to the benefit of and be binding upon successors to the Parties to this Agreement. Neither Party hereto shall assign, transfer or otherwise dispose of any of its rights, title or interest in, to, or under this Agreement without the prior written consent of the other Party. However, either Party shall have the right to assign this Agreement or any of its rights and/or obligations hereunder to any affiliate of said Party, or to any person or entity that acquires all or substantially all of the ownership or equity interests or assets of said party or of any entity that owns or controls, directly or indirectly, substantially all of the ownership or equity interests or assets of said Party, whether by stock purchase, asset purchase, merger, operation of law or otherwise.

12.3 Notices. Notices shall be given by personally delivering or mailing same by certified mail, overnight carrier, or by facsimile transmission, to the respective address or fax number of RCRI and Company set outin the applicable Work Order, or to other addresses or fax numbers as the Parties may specify in writing. Notice shall be deemed to have been given upon delivery, or, by facsimile, upon reception and reproduction in legible form by the fax equipment of the Party to whom the notice is addressed.

12.4 Governing Law and Actions. This Agreement shall be governed, enforced and construed by Minnesota law without giving effect to the principles of conflicts laws thereof. Any legal action arising out of or related to this Agreement shall be brought in an appropriate Minnesota court and the Parties hereby consent to the personal and exclusive jurisdiction and venue of the courts of the State of Minnesota. If the services of an attorney are required to protect the interests of either Party or to collect unpaid fees, the non-prevailing Party agrees to pay all costs and fees, including reasonable attorney fees.

12.5 Force Majeure. Neither Party will be liable for any delay in its performance in the event and to the extent that such performance is delayed or prevented due to causes strictly beyond its reasonable control; provided that such Party promptly notifies the other Party orally and in writing of such delay occasioned by such causes. The Party whose performance is delayed by such an event will use its best efforts to minimize its effect and to eliminate such event insofar as possible with a minimum of delay.

12.6 Severability. If any provision of this Agreement is held to be unenforceable for any reason, it will be modified rather than voided, if possible, in order to achieve the intent of the Parties to this Agreement to the extent possible. Any provision held overbroad as written will be deemed amended to narrow its application to the extent necessary to make the provision enforceable under applicable law, and enforced as amended. In any event, all other provisions of this Agreement will be deemed valid and enforceable to the full extent.

12.7 Judicial Interpretation. In the event this Agreement requires judicial interpretation, it is acknowledged and agreed that both Parties participated in the negotiation and preparation of this Agreement.

12.8 Entire Agreement; Modification and Waiver. This Agreement, including any Work Order(s), represents the entire and exclusive agreement among the Parties concerning the subject

matter hereof and supersedes all prior agreements and communications, whether written or oral, relating thereto. No purported amendment, supplement, modification or waiver of any provision hereof will be binding unless set forth in a written document signed by the Parties (in the case of amendments, supplements or modifications) or by the Party to be charged thereby (in the case of waivers). Any waiver will be limited to the provision hereof and the circumstance or event specifically made subject thereto and will not be deemed a waiver of any other term hereof or the same circumstance or event upon any recurrence thereof. This Agreement may be executed by facsimile or electronic scanning. This Agreement may be executed and delivered in counterparts (including by facsimile or other electronic transmission), each of which shall be deemed an original, but all of which together will constitute one and the same instrument.

Acknowledged and agreed: RCRI and Company have executed this Agreement through their duly authorized representatives

REGULATORY & CLINICAL RESEARCH INSTITUTE, INC.

By: _____

Print Name: Lisa Olson

Title: President

Date: 19 MAR 2018

FEI NUMBER 41-1934394

PHYSEON GMBH

By: Patrick C. Kullmann

Print Name: Patrick C. Kullmann

Title: CEO

Date: 23 March 2018

EXHIBIT A
Fee Schedule, Expenses and Travel policy

For Services rendered to Company, Company agrees to pay RCRI's rates according to the following Fee Schedule:

1. **Year 2018 hourly rates (USD)**

Executive Principal Advisor	375.00
Clinical Sciences	
Senior Biostatistical Principal Advisor	335.00
Senior Contracts Manager	335.00
Senior Clinical Principal Advisor	330.00
Biostatistical Principal Advisor	320.00
Clinical Principal Advisor	310.00
Principal Biostatistician	305.00
Senior Biostatistician	290.00
Contracts Manager	280.00
Principal Clinical Project Manager	275.00
Biostatistician II	275.00
Biostatistician I	255.00
Senior Clinical Project Manager	250.00
Clinical Project Manager	235.00
Principal Clinical Data Manager	230.00
Principal Clinical Research Associate	220.00
Senior Clinical Data Manager	215.00
Clinical Data Manager II	200.00
Senior Clinical Research Associate	195.00
Clinical Data Manager I	180.00
Clinical Research Associate	175.00
Administrative Services	115.00
Regulatory Affairs and Quality Systems	
Senior Regulatory Principal Advisor	330.00
Regulatory Principal Advisor	310.00
Senior Regulatory Project Director	280.00
Regulatory Project Director	260.00
Regulatory Project Manager	250.00
Senior Quality Systems Specialist	240.00
Senior Regulatory Specialist	230.00
Regulatory Specialist	200.00
Regulatory Associate	175.00
Health Economics/Reimbursement	
Senior Health Economic Principal Advisor	335.00
Health Economic Principal Advisor	320.00

2. **Policy for Travel Expenses**

A. For Services requiring travel, RCRI will invoice actual travel time, in addition to time actually worked provided that i) actual travel time and time actually worked will not be billed concurrently (no double billing); ii) if RCRI is performing services for any other party while traveling for Company, RCRI will not invoice Company for such travel time and iii) only intended travel time will be billed (e.g. airlines delays will not be billed).

B. International air travel is in business class.

3. **Other Expenses**

All expenses including travel, long distance telephone charges, photocopying/printing charges, courier charges, direct office supplies and other expenses incurred by RCRI on behalf of Company will be invoiced to Company as provided in Section 3.2 of the Agreement, provided, however, that all such individual expenses of $5,000 (five thousand) or more are approved in writing in advance by Company.

Schedule 1

WORK ORDER FORM

This Work Order is valid only for projects with Companies having a duly mutually-executed Consulting Agreement. Please review, sign, date, and fax back to RCRI at 952-884-6518. Thank you.

☐ New Work Order; Code:	
Contact Name:	Work Order Date:
Company Name:	Phone #:
RCRI Contact Name:	RCRI Project Code:
Project Title:	

Description of Work :

Significant Deliverables/Milestones/Other Project Specifications:	Estimated Timeline:

Estimate:
Estimates are provided for client budgeting purposes. Actual time for work performed will be billed, which may be more or less than the estimate provided here.

☐ Retainer Not Required (RCRI use only)
☐ Retainer Required (RCRI use only): A retainer in the amount of $ is required as part of this work order. Please return this payment with the signed work order. Work will not commence until payment of the retainer is received by RCRI.

Company agrees that upon completion of the above deliverables (unless modified by a subsequent work order), Consultant has fulfilled its obligation under this Work Order. The specifications outlined are based on the project requirements and assumptions set forth herein. Any changes to the project requirements or assumptions may require a new work order. Cost estimates are based on current billing rates. RCRI work orders are valid for a period of 60 days from work order date. This work order is confidential and shall not be discussed with any third party.

Consultant and Company agree to this Work Order. Company hereby authorizes commencement of the Services.

Client Signature:	Date:
RCRI Signature:	Date:

EXHIBIT B
Wire Transfer Information

For Services rendered to Company, Company agrees to make all payments via wire transfer using the following information:

Domestic Wire Transfer Information:

EXHIBIT 2

Veinplicity for Improved Venous Access: The VIVA Trial

Investigational Plan

Physeon GmbH
Herrenacker 15
8200 Schaffhausen
Switzerland

Study ID #PHY0011
Investigational Plan Date: 18 Sep 2018
Version #: 1

List of Abbreviations and Acronyms

AE	Adverse event
CFR	Code of Federal Regulations
CV	*Curriculum Vitae*
CVC	Central venous catheter
DAL	Device Accountability Log
DCF	Data Clarification Form
eCRF	Electronic Case Report Form
EDC	Electronic data capture
eTMF	Electronic trial master file
FDA	Food and Drug Administration
HIPAA	Health Insurance Portability and Accountability Act of 1996
ICF	Informed Consent Form
ID	Identification
IFU	Instructions for Use
IRB	Institutional Review Board
ITT	Intent-to-Treat
IV	Intravenous
mL	Milliliter
NaCl	Sodium chloride
PICC	Peripherally inserted central catheter
PVC	Peripheral vein cannulation
SAE	Serious adverse event
SAP	Statistical Analysis Plan
UADE	Unanticipated adverse device effect

Investigational Plan Synopsis

Study Title	Veinplicity for Improved Venous Access: The VIVA Trial
Study ID	PHY0011
Study Device	Veinplicity.
Control Device	Tourniquet alone.
Study Purpose	To demonstrate that use of Veinplicity improves successful peripheral vein access in enrolled subjects.
Target Indication for Use	Veinplicity is intended to be used to enhance the identification of suitable peripheral veins for the purpose of cannulation.
Study Design	This is a prospective, randomized controlled study that will assess ability of Veinplicity to improve successful peripheral vein access in enrolled subjects. Potential subjects will undergo a peripheral vein assessment by a study clinician, which is standard of care prior to peripheral vein cannulation (PVC) for the establishment of intravenous (IV) access. Adults requiring peripheral intravenous access who are assessed as having "fair or poor" vein quality[1] will be consented, enrolled and randomized into the study. Subjects will be randomized in a 1:1 ratio to either 1) tourniquet alone (control group) or 2) Veinplicity with tourniquet (treatment group). Subjects may undergo up to four attempts at PVC (up to two attempts per study clinician;[2] up to two clinicians per subject) using a 20 or 22 gauge cannula. If successful peripheral vein access after four attempts has not been achieved, the subject will be considered a study failure and may proceed to using an adjunct method (e.g., heat pack, ultrasound, infrared imaging, etc.), and/or a different means of access, such as a peripherally inserted central catheter (PICC) or central venous catheter (CVC), and/or escalation to an IV specialist. Use of an adjunct method, and/or different means of access, and/or escalation to an IV specialist prior to the fourth attempt will be considered a failure for the purpose of the primary endpoint. Clinician and subject satisfaction will be separately assessed using separate surveys on Day 0. Subjects in both groups will be followed for one day (either phone or in-hospital visit) after enrollment for safety. Qualified study clinicians must have at least two years of experience inserting peripheral IVs and must perform at least ten PVCs per week. They cannot currently or previously be on an IV specialist team or be an anesthesia provider. The primary hypothesis to be tested is: Veinplicity with tourniquet is superior to tourniquet alone for successful peripheral vein access when used to cannulate subjects assessed as having a fair or poor level of vein quality. The primary endpoint is first-stick success. It is expected that this study will enroll approximately 246 subjects; 123 per study group. It is expected that

	up to five sites will be involved in this study. A planned interim analysis will be conducted to reassess the study planned sample size when approximately 50% of subjects have been enrolled. Enrollment will not stop during the interim analysis activities. Safety will be evaluated by the collection and analysis of the incidence and severity of all procedure- and/or device-related adverse events through the 1-day post-insertion phone call/visit.
Attempt[2]	Puncture of the skin constitutes one attempt.
Vein Access Success and Failure	Vein Access Success: Defined as obtaining blood flashback in the cannula chamber and successful flushing of the cannula with 3 mL normal saline (0.9% NaCl) to confirm patency, using the approach to which the subject is randomized (maximum 4 attempts). Vein Access Failure: Defined as being unable to successfully cannulate a vein (no flashback obtained and/or unable to successfully flush with 3 mL normal saline) using the approach to which the subject is randomized (maximum 4 attempts). Signs of vein access failure include immediate signs of cannulation site swelling associated with flushing. If an adjunct method, different means of access, and/or an IV specialist are used, the subject is a failure for the primary endpoint.
Primary Study Objective	To demonstrate that Veinplicity with tourniquet is superior to tourniquet alone when used to successfully access a peripheral vein for cannulation in subjects assessed as having a fair to poor level of vein quality.
Primary Study Endpoint	First-stick success
Safety Endpoint	Safety will be evaluated by the collection and analysis of the incidence and severity of all procedure- and/or device-related adverse events through the Day 1 post-insertion phone call/visit.
Additional Study Endpoints	1. Number of attempted sticks to successful vein access. 2. Total procedure time: time from starting skin preparation for the control arm or time from electrode application for the treatment arm, to declaration of study success/failure for the primary endpoint. 3. Time to vein access success: time from tourniquet application after randomization to declaration of study success/failure for the primary endpoint. 4. Subject satisfaction and pain: at the time of vein access success/failure declaration for the primary endpoint. 5. Clinician satisfaction: at the time of vein access success/failure declaration for the primary endpoint. 6. Change in the vein quality score from baseline to post-stimulation: both scores to be assessed at the time of tourniquet application by the same clinician.

Investigational Centers	Up to five centers in the United States will participate in this study.
Study Population	Adults requiring peripheral intravenous access who are assessed as having "fair or poor" vein quality.
Study Duration	It is expected that subjects will be in the study for two consecutive days. Day 0 is the day the PVC is attempted for the primary endpoint and Day 1 is the following day, when the subject will be asked about device- and/or procedure-related adverse events, either via phone call or an in-hospital visit.
Key Inclusion Criteria	1. Subject is ≥ 22 years old. 2. Subject is assessed as having fair or poor vein quality. 3. Subject's both arms are suitable for cannulation. 4. Subject will not suffer harm from a delay in having an IV established as determined by the treating clinician.
Key Exclusion Criteria	1. Subject has existing intravenous access. 2. Subject has a planned or existing intra-arterial access. 3. Subject has broken, infected or irritated skin and/or dermatological conditions, e.g., eczema, psoriasis and/or allergic reactions, on either forearm. 4. Subject has an active implantable medical device. 5. Subject wears a transdermal drug delivery patch on her/his forearm. 6. Subject has, at the site of or in between Veinplicity electrode application sites, an active/suspected malignancy, active/suspected deep vein thrombosis or thrombophlebitis, impaired circulation, impaired sensation, active/uncontrolled bleeding, recently radiated tissue, recent fracture, recent surgery, osteoporosis, localized abscess, localized tuberculosis, and/or a chronic wound with potential underlying osteomyelitis. 7. Subject has impaired cognition or communication (unable to provide accurate feedback). 8. Subject has a documented diagnosis of a history of seizures and/or epilepsy. 9. Subject is pregnant and/or breastfeeding at the time of study enrollment.
Statistical Hypotheses	The primary hypotheses to be tested are as follows: H_0: $P_t - P_c = 0$ H_1: $P_t - P_c \neq 0$ where P_t and P_c are the first-stick success rates for the Veinplicity with touniquet (treatment) and tourniquet alone (control) groups, respectively. If the difference in success rates, $P_t - P_c$, is found to be statistically different than 0, at a significance level (alpha) of 0.05, and $\widehat{P_t} - \widehat{P_c} > 0$, then it will be concluded that the test success rate is higher and success for the primary endpoint achieved.

Statistical Test Method	The primary endpoint of first-stick success will be analyzed by comparing the two success rates with a two-sided normal approximation (Z-test) with pooled standard deviation. If the difference in success rates, $P_t - P_c$ is found to be statistically different than 0, at a significance level (alpha) of 0.05, and $\hat{P}_t - \hat{P}_c > 0$, it will be concluded that Veinplicity with tourniquet is superior to tourniquet alone in achieving vein access success.
Sample Size	Approximately 246 subjects will be enrolled, including a 5% attrition rate and allowing for an interim look for the purpose of sample size re-estimation. Assuming vein access success in the Veinplicity with tourniquet group is 92% and vein access success in the tourniquet alone group is 78%, to demonstrate superiority, 116 treated subjects are needed in each group, for a total of 232 subjects (two-sided alpha = 5%; power = 85%). Assuming a 5% dropout rate, a total of 246 subjects (123 per group) will be enrolled. In order to ensure the study is adequately powered at the conclusion of the trial, an interim analysis will be performed when approximately 50% of subjects (~58 subjects per group) have been assessed for vein access success with a potential for sample size re-estimation. This analysis will be performed for the sole purpose of increasing the study sample size, if necessary. The study sample size may only be held constant or increased; it cannot be reduced. The study will not be stopped early for success, and no hypothesis testing will be performed at the time of sample size re-estimation. The approach to the sample size re-estimation will be based upon the methods of Mehta and Pocock[3] and will be conducted by an independent statistician who is not a member of the study team. If the conditional power is 'promising,' the sample size may be increased up to a maximum of 492 (2.0 x the initial estimated sample size). Enrollment will not cease during interim analysis activities and the interim analysis will not affect the study power calculation.
Sponsor	Physeon GmbH Herrenacker 15 8200 Schaffhausen, Switzerland
Study Management Center	Regulatory and Clinical Research Institute, Inc. (RCRI®) 5353 Wayzata Boulevard, Suite 505 Minneapolis, Minn. 55416

1. Background

The current practice for gaining peripheral venous access has not changed significantly in over 80 years: use of a tourniquet followed by flexing of the digits to trap blood in the veins. These actions cause the veins to distend and increase in prominence. In most cases, this approach is sufficient. However, venous access is problematic in certain subjects, resulting in multiple attempts by the practitioner to gain access. Placement of peripheral intravenous (IV) catheters is a very common procedure in multiple healthcare settings. The traditional method of peripheral vein cannulation (PVC) includes palpating or direct visualization of the target vein for cannulation. It is not uncommon for subjects to lack visual or palpable veins ideal for successful cannulation. Previous medical history, body type including obesity, drug use, fluid status, and age can be challenges for successful cannulation. Blind insertion of peripheral IV catheters, besides being potentially painful and time-consuming, may result in arterial puncture, nerve damage and paresthesia.[4] Repeated attempts, often requiring multiple practitioners, can lead to delays in diagnosis and treatment and increase the risk of both mechanical and infectious complications.[4-6]

Veinplicity by Physeon GmbH is an electrical stimulation device that is designed to increase local intravascular blood volume and therefore improve a practitioners' ability to gain intravenous access. The increased circulation results from provoked muscle stimulation. As a class of devices, non-implanted electrical stimulation devices carry a well-documented safety profile. As a result, the risks associated with devices in this category are well-known, understood and fall into the low-risk category.

2. Device Description

2.1 Investigational Device: Veinplicity

Veinplicity is a reusable electrical stimulation device consisting of a battery-operated, adjustable control unit, reusable main cable and disposable connective leads with two patch-style electrodes (See Figures 1 and 2). The control unit, main cable and test cable are reusable. The batteries in the control unit are replaceable. A test cable is provided to test the stimulator to assess functionality and need for maintenance or replacement of the control unit. All components are provided non-sterile.

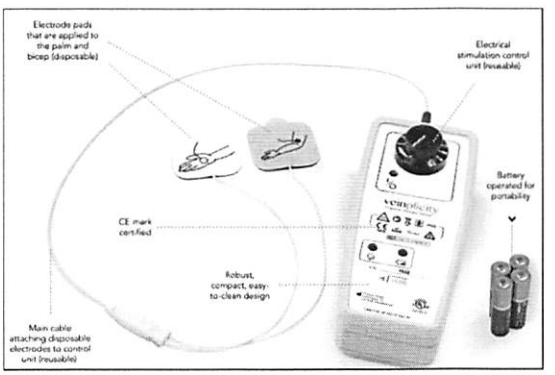

Figure 1. Veinplicity System Components

To use the device (see Figure 2), electrodes are placed on the arm (white electrode patch on the palmar surface of the hand and the blue electrode patch on the bicep of the arm) and connected to the stimulator using the main cable. The unit is turned on and off manually.

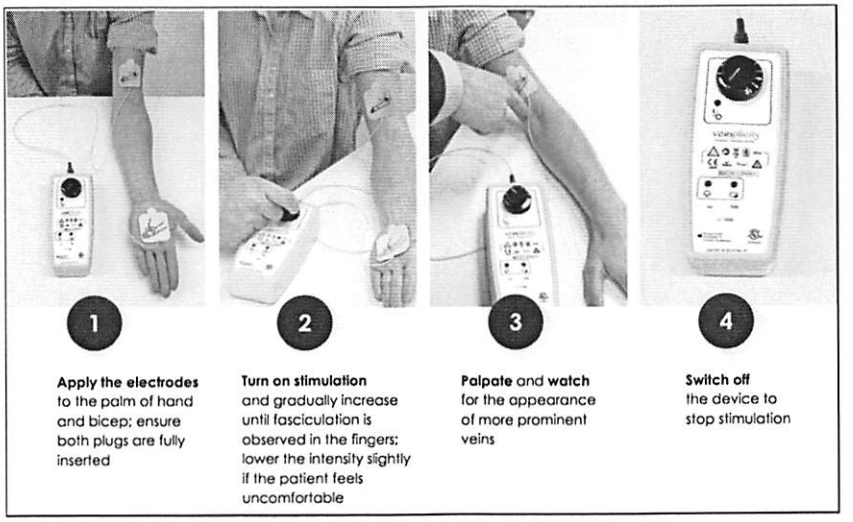

Figure 2. Veinplicity Electrode Placement and Use

Veinplicity stimulation is administered for at least 2 minutes but not longer than 10 minutes. Stimulation continues until a suitable access site is identified, based on clinician's discretion. The device automatically switches off after 15 minutes of stimulation. Subsequent to stimulation, the clinician applies a tourniquet and peripheral intravenous cannulation is performed according to normal practice guidelines.

2.2 Target Indication for Use

Veinplicity is intended to be used to enhance the identification of suitable peripheral veins for the purpose of cannulation.

2.3 Control Device: Tourniquet Alone

The control device for this study is the standard tourniquet used alone to promote vascular distention by impeded venous flow while maintaining arterial circulation. The tourniquet is a single-use, non-sterile device.

3. Study Design

3.1 Study Design

This is a prospective, randomized controlled study that will assess ability of Veinplicity to improve successful peripheral vein access in enrolled subjects. Potential subjects will undergo a peripheral vein assessment by a study clinician, which is standard of care prior to peripheral vein cannulation (PVC) for the establishment of intravenous (IV) access. Adults requiring peripheral intravenous access who are assessed as having "fair or poor" vein quality1 will be consented, enrolled and randomized into the study. Subjects will be randomized in a 1:1 ratio to either 1) tourniquet alone (control group) or 2) Veinplicity with tourniquet (treatment group). Subjects may undergo up to four attempts at PVC (up to two attempts per study clinician; up to two clinicians per subject) using a 20 or 22 gauge cannula. If successful peripheral vein access after four attempts has not been

achieved, the subject will be considered a study failure and may proceed to using an adjunct method (e.g., heat pack, ultrasound, infrared imaging, etc.), and/or a different means of access, such as a peripherally inserted central catheter (PICC) or central venous catheter (CVC), and/or escalation to an IV specialist. Use of an adjunct method, and/or different means of access, and/or escalation to an IV specialist prior to the fourth attempt will be considered a failure for the purpose of the primary endpoint. Clinician and subject satisfaction will be separately assessed on Day 0. Subjects in both groups will be followed for one day (either phone or in-hospital visit) after enrollment for safety. Qualified study clinicians must have at least two years of experience inserting peripheral IVs and must perform at least ten PVCs per week. They cannot currently or previously be on an IV specialist team or be an anesthesia provider. The primary hypothesis to be tested is: Veinplicity with tourniquet is superior to tourniquet alone for successful peripheral vein access when used to cannulate subjects assessed as having a fair or poor level of vein quality. The primary endpoint is first-stick success. It is expected that this study will enroll approximately 246 subjects; 123 per study group. It is expected that up to five sites will be involved in this study. A planned interim analysis will be conducted to reassess the study planned sample size when approximately 50% of subjects have been enrolled. Enrollment will not stop during the interim analysis activities. Safety will be evaluated by the collection and analysis of the incidence and severity of all procedure- and/or device-related adverse events through the 1-day post-insertion phone call/visit.

3.2 Study Purpose

To demonstrate that use of Veinplicity improves successful peripheral vein access in enrolled subjects.

3.3 Primary Study Objective

To demonstrate that Veinplicity with tourniquet is superior to tourniquet alone when used to successfully access a peripheral vein for cannulation in subjects assessed as having a fair to poor level of vein quality.

3.4 Primary Study Endpoint

First-stick success.

3.5 Safety Endpoint

Safety will be evaluated by the collection and analysis of the incidence and severity of all procedure- and/or device-related adverse events through the Day 1 post-insertion phone call/visit.

3.6 Additional Study Endpoints

1. Number of attempted sticks to successful vein access.
2. Total procedure time: time from starting skin preparation for the control arm or time from electrode application for the treatment arm, to declaration of study success/failure for the primary endpoint.
3. Time to vein access success: time from tourniquet application after randomization to declaration of study success/failure for the primary endpoint.
4. Subject satisfaction and pain: at the time of vein access success/failure declaration for the primary endpoint.
5. Clinician satisfaction: at the time of vein access success/failure declaration for the primary endpoint.

6. Change in the vein quality score from baseline to post-stimulation: both scores to be assessed at the time of tourniquet application by the same clinician.

3.7 Definition of Attempt

Puncture of the skin constitutes one attempt.

3.8 Vein Access Success and Failure

Vein Access Success: Defined as obtaining blood flashback in the cannula chamber and successful flushing of the cannula with 3 mL normal saline (0.9% NaCl) to confirm patency, using the approach to which the subject is randomized (maximum 4 attempts).

Vein Access Failure: Defined as being unable to successfully cannulate a vein (no flashback obtained and/or unable to successfully flush with 3 mL normal saline) using the approach to which the subject is randomized (maximum 4 attempts). Signs of vein access failure include immediate signs of cannulation site swelling associated with flushing. If an adjunct method, different means of access and/or an IV specialist are used, the subject is a failure for the primary endpoint.

Cannulation attempts may be made in one or both arms; however, an individual clinician can only make up to 2 total attempts and the subject can only have up to 4 total attempts between both arms to determine study success or failure.

4. Investigational Study Centers

Up to five centers in the United States will participate in this study. Each site will identify a study investigator who is responsible for study oversight and management. This role does not need to be fulfilled by a physician, i.e., a registered nurse may be the site investigator.

5. Study Population

The study population will consist of adults requiring peripheral intravenous access who are assessed as having "fair or poor" vein quality.

5.1 Inclusion Criteria

All criteria must be answered as "yes" for study enrollment:

1. Subject is $\geq$ 22 years old.
2. Subject has been assessed as having fair or poor vein quality.
3. Subject's both arms are suitable for cannulation.
4. Subject will not suffer harm from a delay in having an IV established as determined by the treating clinician.
5. Subject is willing and able to give informed consent and HIPAA authorization.
6. Subject is willing and able to complete all study requirements, including completion of the Subject Satisfaction Scale on Day 0 and the Day 1 post-procedure AE assessment phone call/visit.

5.2 Exclusion Criteria

All criteria must be answered as "no" for study enrollment:

1. Subject has existing intravenous access.
2. Subject has a planned or existing intra-arterial access.
3. Subject has broken, infected or irritated skin and/or dermatological conditions, e.g., eczema, psoriasis and/or allergic reactions, on either forearm.

4. Subject has an active implantable medical device.
5. Subject wears a transdermal drug delivery patch on her/his forearm.
6. Subject has, at the site of or in between Veinplicity electrode application sites, an active/suspected malignancy, active/suspected deep vein thrombosis or thrombophlebitis, impaired circulation, impaired sensation, active/uncontrolled bleeding, recently radiated tissue, recent fracture, recent surgery, osteoporosis, localized abscess, localized tuberculosis, and/or a chronic wound with potential underlying osteomyelitis.
7. Subject has impaired cognition or communication (unable to provide accurate feedback).
8. Subject has a documented diagnosis of a history of seizures and/or epilepsy.
9. Subject is pregnant and/or breastfeeding at the time of study enrollment.
10. Subject, in the opinion of the investigator, should be excluded from the study.

5.3 Assessment of Vein Quality

The vessel assessment scale provided in Table 1 will be used in this study to categorize peripheral vessel quality. This assessment is performed with a tourniquet placed as per standard-of-care on the upper arm. Vein quality will be assessed at baseline and again after tourniquet application in both randomization groups. The same clinician should perform the baseline and post-tourniquet application vein quality assessments for consistency.

Table 1: Vessel Health and Preservation (VHP) Peripheral Vein Assessment Scale

Grade	Vein Quality	Definition of Vein Quality
1	Excellent	4-5 palpable/easily visible veins suitable to cannulate
2	Good	2-3 palpable/visible veins suitable to cannulate
3	Fair	1-2 palpable/visible veins suitable to cannulate (veins may be small, scarred or difficult to find and require heat packs to aid vasodilation)
4	Poor	Veins not palpable/visible (requires ultrasound assistance or infrared viewer)
5	None Identifiable	No visible (naked eye or aids) or palpable veins

People assessed as having vessels that are fair or poor indicate to the clinician that cannulation may be challenging and require extra time or resources. In these cases, use of Veinplicity may increase vessel size and therefore improve identification of vessels suitable for cannulation. These subjects represent the target group for use of Veinplicity.

6. Informed Consent

After assessment of vein quality, potential study subjects must document their consent for study participation and authorization for use and disclosure of health information by signing the study-specific IRB-approved Informed Consent Form (ICF). As part of the consent process, the subject will have the opportunity to ask questions of and receive answers from site personnel conducting the study. Subjects will be considered to be enrolled in the study once they have signed the ICF, it is confirmed that they meet all inclusion/exclusion criteria and they are randomized to a study arm. A person can only be treated under this study's

investigational plan one time, i.e., they cannot be re-treated as part of the study once they have been declared a study success or failure.

7. Study Procedures

7.1 Study Flow Diagram and Schedule of Procedures

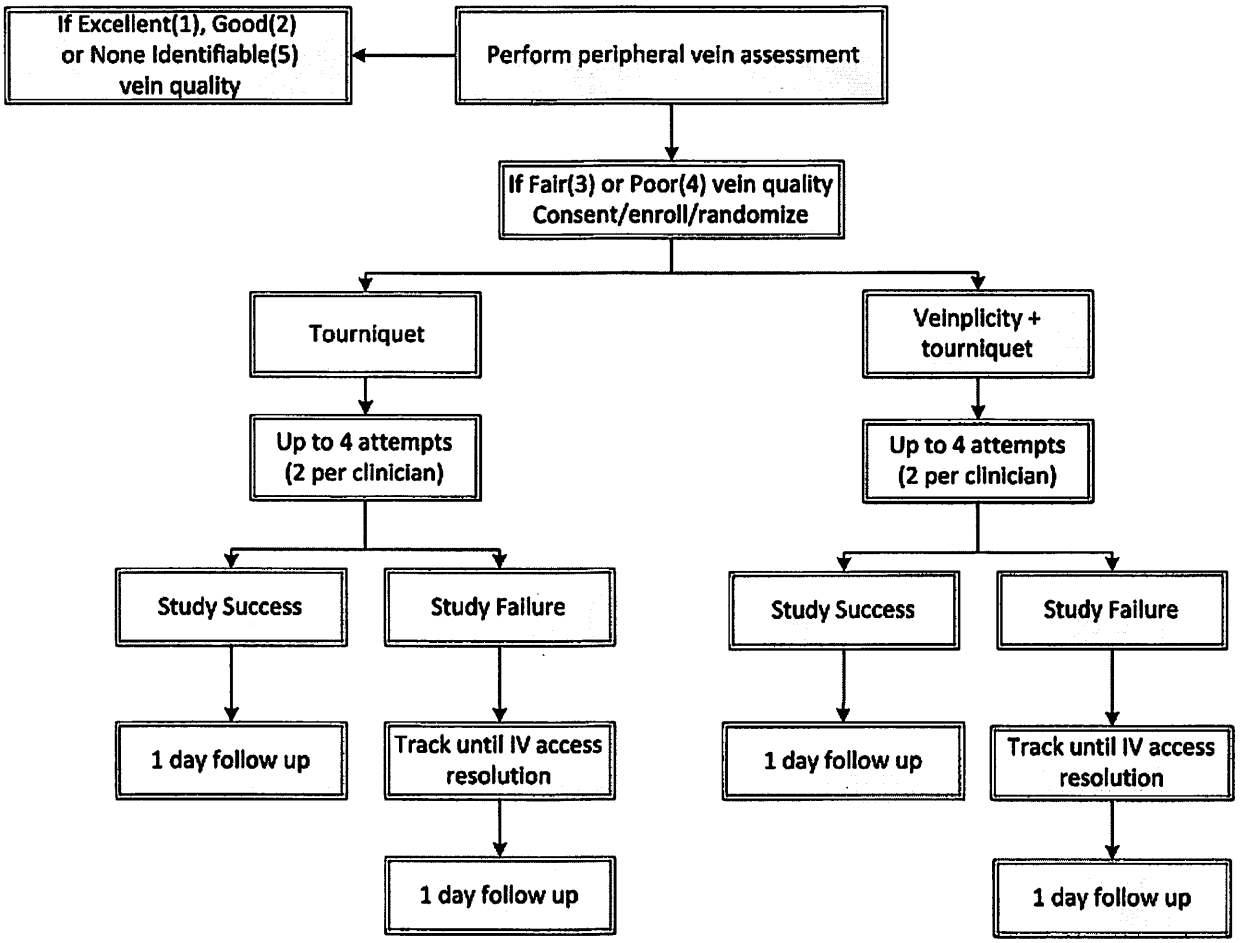

Figure 3. Veinplicity Study Flow

Table 2. Schedule of Study Procedures

Activity	Procedure Day (Day 0)	Post-procedure (Day 1)
Vein Quality Assessment	X	
Informed Consent	X	
Inclusion/Exclusion Criteria	X	
Pregnancy Test (if applicable)	X	
Randomization	X	
Demographics	X	
Relevant Medical History	X	
Assigned Treatment	X	
Post-Tourniquet Vein Quality Assessment	X	
Subject Satisfaction Survey	X	
Clinician Satisfaction Survey	X	
Adverse Event Assessment	X	X

7.2 Procedure Day (Day 0)

7.2.1 Vein Quality Assessment

Prior to consent, as part of standard-of-care practice, vein quality will be assessed by trained study personnel with a tourniquet applied to the upper arm(s). If vein quality is determined to be excellent, good, or none identifiable (see Table 1), the potential subject will not be consented for study participation. If it is determined that they have veins that meet the criteria for fair or poor, they will be consented and assessed for inclusion/ exclusion criteria. The vein quality assessment score will be recorded on the Procedure Worksheet.

7.2.2 Informed Consent

Potential study candidates will be consented for study participation as described in Section 6, Informed Consent, after it is determined that their vein quality is assesses as fair or poor per Table 1 and Section 7.2.1.

7.2.3 Inclusion/Exclusion Criteria Assessment

After consenting, the remaining inclusion/exclusion criteria (Section 5) will be assessed. A pregnancy test (in-clinic urine stick) is to be performed on all women of child-bearing potential. If the subject meets all criteria, they will proceed to study randomization. If not, they will be exited from the study.

7.2.4 Randomization

Prior to enrollment of the first subject, the randomization scheme will be set up by the study statistician in the study database for access by a site at the time of randomization. After enrollment, subjects will be randomized according to a pre-specified two-tiered randomization schedule. Subjects will first be classified by vein quality assessment: fair or poor. Then, within that vein quality assessment group, they will be randomized to either the treatment arm (Veinplicity with tourniquet) or the control arm (tourniquet alone) in a 1:1 ratio. The

randomization will be based on random, permuted blocks and stratified by study site and vein quality assessment. In the event a subject is randomized but is not treated according to their randomization assignment, that subject's randomization will not be reused and the site will go to the next sequential subject number for the next subject to be randomized.

Trained site personnel will access the study database, which will assign the subject to the treatment arm or the control arm as indicated by the pre-specified randomization scheme. Study clinicians cannot influence a subject's assignment.

7.2.5 Demographics and Relevant Medical History

Demographic and relevant medical history information should be gathered from the subject before cannulation is attempted; however, if cannulation must immediately proceed, this information can be obtained after the study procedure. Relevant medical history will be gathered for the following conditions: history of difficult venous access, diabetes mellitus, intravenous drug use (prescribed including chemotherapy or illicit), vascular disease, smoking, and renal insufficiency.

7.2.6 Assigned Treatment

Subjects will be randomized to either the treatment arm (Veinplicity with tourniquet) or the control arm (tourniquet only). For all subjects, assess both arms for cannulation suitability. Skin preparation will be performed in accordance with the site's standard practice.

NOTE: *For subjects who are stimulated by the Veinplicity device, do not draw blood samples during the cannulation procedure, as it is not known if the device will affect blood test results. If blood is inadvertently drawn during the cannulation procedure for subjects treated with Veinplicity, discard the blood sample(s).*

Veinplicity with Tourniquet (Treatment Group)

1. The clinician is to remain with the subject during and after stimulation. Refer to the Veinplicity Instructions for Use (IFU) for complete information.
2. Place the Veinplicity electrodes on the selected arm for cannulation. Place the white electrode patch on the palmar surface of the hand and the blue electrode patch on the bicep of the arm (Figure 2). Electrodes can be placed in any orientation as long as the location is maintained. Connect the electrodes to the stimulator using the main cable.
3. Turn Veinplicity on by turning the dial to #1 and observing for a physical response (muscle fasciculation). If muscle fasciculation is not observed, steadily increase the intensity by turning the dial to the maximum level comfortably tolerated by the subject. The subject will experience tingling but the sensation should not be painful. If the sensation is not tolerable, the intensity must be lowered by turning the dial down to a tolerable level that still produces muscle fasciculation.

4. Maintain this intensity for a minimum of 2 minutes and a maximum of 10 minutes, until the target vein becomes visible or palpable. Turn the device off by rotating the dial counter-clockwise until the on/off light turns off.
5. The site's standard cannulation procedure, i.e., skin cleansing and tourniquet application, is performed. Apply the tourniquet to the same arm that was stimulated with Veinplicity; re-assess and document vein quality post-stimulation and record this value on the Procedure Worksheet, then proceed with cannulation.
6. One clinician may make up to two attempts at cannulation. If cannulation is not achieved (flashback obtained and successfully flushed with 3 mL of normal saline without swelling) after two attempts, a second clinician will replace the first and up to two more attempts may be made. All attempts on one arm should be made within 5 minutes of stimulation cessation.
7. If the clinician elects to switch to the other arm to attempt cannulation, Veinplicity must be reapplied to the second arm as described in steps 1-5 above. The same set of electrodes used on the first arm are to be used again on the second arm; do not use a new set of electrodes.
8. If the subject is successfully cannulated (flashback obtained and able to flush with 3 mL normal saline without swelling) in 4 or fewer total attempts, i.e. four attempts total between both arms, the subject is considered to be a success for this study. If the subject is not successfully cannulated (no flashback obtained and/or unable to successfully flush with 3 mL normal saline) in 4 or fewer total attempts between both arms, they are considered to be a study failure and alternative methods of achieving IV access may be used.
7. After declaration of study success or failure, remove the electrodes.
8. Clean and disinfect Veinplicity after each subject as per the Instructions for Use.

In summary, Veinplicity stimulation is to be administered only once to each arm; however, both arms may be stimulated sequentially if necessary. Cannulation attempts in an arm must completed within 5 minutes of stimulation cessation in that arm. An individual clinician an only make up to 2 total attempts at cannulation, and the subject can only have up to 4 total attempts between both arms to determine study success or failure.

Tourniquet Only (Control Group)

Intravenous cannulation will be attempted for control group subjects using only a tourniquet after standard-of-care skin preparation. Baseline and post-tourniquet vein quality assessments are to be performed, preferably by the same clinician. A clinician may make up to 2 attempts at cannulation. If cannulation is not achieved after 2 attempts, a second clinician will replace the first and up to 2 more attempts may be made. If the subject is successfully cannulated in 4 or fewer attempts, the subject is considered to be a success for this study. If the subject is not successfully cannulated in 4 or less attempts, they are considered to be a study failure and alternative methods of achieving IV access may be used. Both arms may be used for cannulation attempts, but an individual clinician can only make up

to 2 total attempts and the subject can only have up to 4 total attempts between both arms to determine study success or failure.

7.2.7 Procedure Measurements

The following data points will be collected on the Procedure Worksheet:

1. All subjects:
   a. Total procedure time: time from starting skin preparation for the control arm or time from electrode application for the treatment arm, to declaration of study success/failure for the primary endpoint.
   b. Time from tourniquet application after randomization to the time of vein access success/failure declaration for the primary endpoint.
2. Veinplicity group only:
   a. Time the first Veinplicity electrode is applied to the subject's arm to the time of vein access success declaration for the primary endpoint.
   b. Time the Veinplicity device is turned on to the time it is turned off (stimulation duration). If Veinplicity is switched from one arm to the other, mark the time from the second time it is turned on to the second time it is turned off.
   c. Stimulation intensity (dial setting(s)); treatment group only.

7.2.8 Subject Satisfaction Survey

On Day 0, after the subject is declared either a study success or failure, they will complete the Subject Satisfaction Survey to assess their satisfaction with the assigned cannulation approach. The survey will also include an assessment of pain related to the use of the device (treatment group) and pain associated with IV catheter placement (both treatment and control groups).

7.2.9 Clinician Satisfaction Survey

On Day 0, after cannulation has been attempted and the subject is declared either a study success or failure, the clinician(s) will complete the Clinical Satisfaction Survey to assess their satisfaction with the assigned cannulation approach and their perception of each subject's experience. Each clinician will complete her/his own Clinical Satisfaction Survey.

7.2.10 Adverse Event Assessment

An assessment of the subjects for adverse events will be performed after the cannulation procedure is completed on Day 0 and via phone call or in-hospital visit on Day 1; see Section 8.

7.3 Post-procedure (Day 1)

On Day 1, study personnel will contact a subject to assess if any adverse events related to the assigned cannulation approach and/or study device have occurred; see Section 8. This can be done via phone call or an in-hospital visit, at the discretion of the study personnel performing the assessment. A script will be used to guide the discussion with the subject to help ensure the consistent and accurate collection of information.

7.4 Study Completion

A subject's participation in the study will be considered complete once they have completed their post-procedure (Day 1) AE assessment.

7.5 Economic Information

Physeon will collect data on the technical and equipment aspects of the cannulation procedure and study personnel in support of the assessment of Veinplicity's economic value. Economic information will be collected on the Procedure Worksheet provided by Physeon.

8. Adverse Events

8.1 Definitions

8.1.1 Adverse Event

An adverse event (AE) is any undesirable/unusual medical experience that occurs to a subject during the study. For the purposes of this study, the investigator is only required to report adverse events that may be related to the cannulation procedure and/or device. If an investigator is unsure about whether to report a finding as an adverse event, s/he should report the event on the AE eCRF in electronic data capture (EDC) system.

8.1.2 Serious Adverse Event

A serious adverse event (SAE) is an adverse event that:

- Leads to death, or
- Leads to serious deterioration in the health of a subject that:
  - results in a life-threatening illness or injury,
  - results in permanent impairment of a body structure or body function,
  - requires inpatient hospitalization ≥ 24 hours or prolongation of existing hospitalization,
  - results in medical or surgical intervention to prevent permanent impairment to a body structure or a body function.

8.1.3 Anticipated Adverse Events

These events may occur as a result of the use of a tourniquet, cannulation, and/or Veinplicity:

- Bruising
- Hematoma
- Bleeding
- Nerve damage
- Skin irritation
- Skin burns
- Inflammation
- Temporary discomfort
- Muscle fatigue and/or soreness
- Pain at the cannula insertion site
- Pain from the tourniquet
- Reaction to the skin preparation solution or process

8.1.4 Unanticipated Adverse Device Effect

An unanticipated adverse device effect (UADE) is defined as any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of study subjects.

8.1.5 Adverse Event Reporting - Site

Adverse events (AEs; see Section 8.1.1) are to be reported in the EDC and are to be updated with new information and upon final resolution of the event. Supporting source documents for AEs may be requested by RCRI; these documents are to be de-identified, labeled with the subject's study identification (ID) number, and uploaded by the site to the EDC system. The investigator will report any suspected UADE to the EDC system and reviewing IRB within ten working days of discovery.

Adverse events will be evaluated by the investigator and classified for seriousness (as defined in Section 8.1.2), relatedness, and severity:

Relatedness

Adverse events will be judged by the investigator as to their relatedness to the study devices (Veinplicity and/or tourniquet) and/or cannulation procedure using the following classifications:

- Possibly Related: The event has a strong temporal relationship to the study devices or procedure and alternative etiology is equally or less likely compared to the potential relationship to the study devices or procedure.
- Probably Related: The event had a strong temporal relationship to the study devices or procedure and another etiology is unlikely.
- Definitely Related: The event is clearly caused by the study devices or procedure and another etiology is unlikely.
- Unknown: Relationship of the event to study devices or procedure and alternative etiology is unknown.

Severity

Adverse events will be categorized by the investigator as mild, moderate, or severe, depending on the event's impact on the subject's daily activity level:

- Mild: Usually transient, requiring no special treatment; does not interfere with the subject's daily activities.
- Moderate: Low-level inconvenience or concern to the subject; may interfere with daily activities, usually resolved by simple therapeutic non-interventional methods.
- Severe: Interruption in subject's daily activity requiring systemic drug therapy or other treatment.

8.1.6 Adverse Event Reporting - Sponsor

The sponsor will notify FDA of a suspected or known UADE within ten working days after discovery and will submit additional reports of its evaluation

and response(s) to FDA requests, if applicable. Adverse events will be reported in the final clinical study report.

9. Statistical Considerations

Please see the separate Statistical Analysis Plan for details about the statistical analyses.

9.1 Sample Size

Approximately 246 subjects will be enrolled, including a 5% attrition rate and allowing for an interim look for the purpose of sample size re-estimation.

Assuming vein access success in the Veinplicity with tourniquet group is 92% and vein access success in the tourniquet alone group is 78%, to demonstrate superiority, 116 treated subjects are needed in each group, for a total of 232 subjects (two-sided alpha = 5%; power = 85%). Assuming a 5% dropout rate, a total of 246 subjects (123 per group) will be enrolled.

In order to ensure the study is adequately powered at the conclusion of the trial, an interim analysis will be performed when approximately 50% of subjects (~58 subjects per group) have been assessed for vein access success with a potential for sample size re-estimation. This analysis will be performed for the sole purpose of increasing the study sample size, if necessary.

The study sample size may only be held constant or increased; it cannot be reduced. The study will not be stopped early for success, and no hypothesis testing will be performed at the time of sample size re-estimation. The approach to the sample size re-estimation will be based upon the methods of Mehta and Pocock[3] and will be conducted by an independent statistician who is not a member of the study team. If the conditional power is 'promising,' the sample size may be increased up to a maximum of 492 (2x the initial estimated sample size). Enrollment will not cease during interim analysis activities and the interim analysis will not affect the study power calculation. Further details regarding the interim analysis, sample size re-estimation and decision process can be found in the separate Statistical Analysis Plan.

9.2 Statistical Hypotheses

The primary hypotheses to be tested are as follows:

H_0: $P_t - P_c = 0$

H_1: $P_t - P_c \neq 0$

where P_t and P_c are the first-stick success rates for the Veinplicity with tourniquet (treatment) and tourniquet alone (control) groups, respectively. If the difference in success rates, $P_t - P_c$, is found to be statistically different than 0, at a significance level (alpha) of 0.05 and $\widehat{P_t} - \widehat{P_c} > 0$, then it will be concluded that the test success rate is higher and success for the primary endpoint is achieved.

9.3 Statistical Test Method

The primary endpoint of first-stick success will be analyzed by comparing the two success rates with a two-sided normal approximation (Z-test) with pooled standard deviation. If the difference in success rates, Pt – Pc is found to be statistically different than 0, at a significance level (alpha) of 0.05, and $\widehat{P}_t - \widehat{P}_c > 0$, it will be concluded that Veinplicity is superior to tourniquet in achieving vein access success.

9.4 Other Statistical Considerations

9.4.1 Analysis Data Set

This study will have one analysis data set, the Intent-to-Treat (ITT) analysis set, which will include all randomized subjects.

9.4.2 Justification of Pooling Data across Centers

A formal analysis will be conducted to determine the appropriateness of pooling data across the study centers. This analysis will include constructing a logistic regression model for the primary effectiveness endpoint with three factors: center, treatment and center by treatment interaction.

9.4.3 Verification of Randomization Procedure

In order to verify the success of the randomization procedure, the distribution of each baseline and demographic variable of interest will be summarized by treatment group. Continuous variables will be summarized via mean, median, standard deviation, and range. Categorical variables will be summarized via counts and frequency distributions.

9.4.4 Missing Data

A sensitivity analysis will be performed for the primary endpoint to assess the potential impact of missing data on the results. A detailed description of the planned sensitivity analysis can be found in the Statistical Analysis Plan together with the analysis of the primary endpoint. Missing values will be ignored for the summaries of baseline characteristics, other summaries and safety endpoints.

9.4.5 Standard Statistical Methods

Unless otherwise stated, all *P*-values will be considered significant at a two-sided significance level of 0.05. Summary statistics will be generated for all relevant variables. In the comparison of continuous variables, distributions will be tested for the normality assumption. If standard parametric techniques are found to be inadequate, an appropriate non-parametric technique or a Box-Cox transformation will be used. No corrections will be made for multiple testing procedures. All analyses will be conducted using SAS® version 9.1 or higher.

10. Study Administration

10.1 Institutional Review Board (IRB) Approval

The study must be reviewed and approved by the site's IRB before subject enrollment begins at the site.

A copy of the IRB approval and IRB-approved ICF/HIPAA form must be submitted to RCRI. Investigators are responsible for submitting and obtaining initial approval and continuing approval from the IRB and forwarding copies of the approval letters and ICF/HIPAA forms to RCRI. The investigator will notify RCRI within five (5) working days in the event of withdrawal of IRB approval.

10.2 Clinical Trial Agreement and Financial Disclosure

The investigator agrees to be responsible for conducting this study in accordance with the signed clinical trial agreement and this investigational plan, including study team oversight/management, reporting and record-keeping requirements and controlling the study devices. In addition, the investigator is responsible for ensuring that proper informed consent is obtained from each subject prior to participating in the study as well as protecting the rights, safety and welfare of participating subjects.

All investigators will be required to sign a financial disclosure form, which certifies the investigator's and his/her immediate family's financial interest in the study sponsors and study outcomes. Investigators must inform RCRI of any changes related to financial disclosure throughout the course of the study and for a period of two years after the study is terminated.

10.3 Subject Confidentiality

All information and data sent to RCRI, the study sponsors and/or their designees concerning subjects and their participation in this study are considered confidential by RCRI, the study sponsors and their designees (subcontractors or contract research organization). Only authorized RCRI and sponsor personnel or approved contracted agents will have access to confidential files and will act in accordance with applicable regulations as required by HIPAA. The FDA and IRB also have the right to inspect and copy all records pertinent to this study.

10.4 Site Qualification

Investigational site qualification visits or phone calls will be conducted by RCRI prior to acceptance of a site into this study. The site qualification visit/call will be scheduled to include time with the investigator, co-investigators, study coordinator and other study personnel. A written report of the qualification visit/call will be drafted by RCRI. Resolution of any concerns and/or completion of any necessary activities identified during the visit/call will be documented and submitted to the investigator.

10.5 Site Training

Study-specific training of study personnel is the responsibility of RCRI and the investigator. Study training will occur before first enrollment. To ensure investigational plan compliance as well as accurate data collection, site training will include a detailed review of the investigational plan, eCRF completion, study-specific procedures, Veinplicity and monitoring logistics.

10.6 Device Accountability

Note: Veinplicity must not be used on a non-study subject. It is the investigator's responsibility to ensure that all Veinplicity units are to kept in a secure location with access limited to authorized study personnel only. All Veinplicity units must be kept at the site until their return is requested by the sponsor.

Veinplicity will be shipped to an investigational site once it has completed site initiation training and uploaded all required study documentation into the electronic trial master file (eTMF). Shipping records will be kept by Physeon detailing the lot number of each device and the date of shipment to the site. Upon receipt, the study coordinator will complete the Device Accountability Log (DAL), documenting receipt of each device unit by lot number and date of receipt. All entries on the DAL must be dated and signed.

The control device is an off-the-shelf tourniquet. A Veinplicity unit that appears to have design or performance issues is to be recorded on the device deficiency eCRF and returned directly to Physeon after receiving approval and instructions from the sponsor.

The DAL, shipping records and device inventory will be reviewed and reconciled during monitoring visits. All Veinplicity units and copies of the DAL will be collected at the end of the study.

10.7 Monitoring

This study will be conducted and monitored in accordance with applicable FDA regulations for IDE studies including 21 CFR 50, 54 and 812; this investigational plan; HIPAA; and RCRI standard operating procedures.

The study site will undergo monitoring visits for evaluation of appropriate conduct and documentation of informed consent, timeliness of data form completion, data accuracy, traceability of investigational devices, and investigational plan and regulatory compliance.

The eCRFs will be reviewed for completeness and accuracy at the investigational site and remotely through the eTMF by RCRI. Information on the eCRFs will be compared to information originally recorded on source documents (i.e. professional notes, study-specific worksheets, etc.). In the event that information on the CRF does not match the corresponding information on the source document, a data clarification form (DCF) for site resolution will be generated.

The monitor may request further documentation, such as clinic notes or lab reports, when adverse events, complications, or malfunctions are observed and reported.

The site will receive a follow-up letter and/or email regarding action points and corrective actions that must be addressed before the next monitoring visit. Documented site noncompliance will be subject to corrective action. If corrective actions are not undertaken or are ineffective, the clinical site may be withdrawn from the study by the sponsor, and devices will be returned to the sponsor.

10.8 Data Management

Study-specific eCRFs will be used to enter study data into the EDC system. Designated study personnel at each site are responsible for entering data into the CRFs. Queries/corrections will be managed within the EDC system via electronic queries. Prior to

final database lock, the investigator will electronically sign each eCRF; this responsibility cannot be delegated to another person.

Data and eCRFs will be reviewed by RCRI at regular intervals throughout the study as outlined in the study monitoring plan. Data clarification requests (DCFs or queries) may be generated by a monitor during a monitoring visit and/or during remote data review. Data management, including DCFs, will be conducted in accordance with the study's Data Management Plan.

10.9 Electronic Trial Master File

This study will utilize an electronic trial master file (eTMF, also known as a "regulatory binder") for the management of all study-related documents that are required by federal law and good clinical practices. The eTMF is the official repository of study documents and will be reviewed by FDA during a Bioresearch Monitoring (BIMO) program inspection, should one occur. The eTMF will be routinely monitored both remotely and during onsite monitoring visits. It is the site's responsibility to ensure all required study documents are complete and uploaded to the eTMF in a timely manner.

10.10 Investigator Responsibilities

The investigator is responsible for ensuring that the study is conducted according to the Clinical Trial Agreement, the investigational plan, IRB requirements and HIPAA. Specific investigator responsibilities are listed in the Clinical Trial Agreement and this investigational plan.

Records and reports must remain on file at the investigational site for a minimum of two years after the completion/termination of this study or Veinplicity approval by FDA, whichever is later. They may be discarded only upon written approval from the sponsor. The sponsor must be contacted if the investigator plans to leave the site to ensure that arrangements for a new investigator or records transfer are made prior to the investigator's departure.

10.11 Investigator Records

Records to be maintained by the investigator may include, but are not limited to:

- Investigational plan and all amendments
- Signed Clinical Trial Agreement
- Signed Financial Disclosure Forms
- IRB approval letter including consent and HIPAA authorization form(s)
- IRB Membership list or Letter of Assurance
- All correspondence relating to the study between the site and study sponsors and/or RCRI
- *Curriculum Vitae* (CVs) and professional licenses for all investigators and licensed study clinicians.
- Site personnel signature and responsibility list
- Clinical monitor sign-in log
- Subject screening log
- The following records will be maintained for each subject enrolled in the study:
  - Subject-signed ICFs and HIPAA forms, and documentation of the consenting process
  - Compete, accurate and current source documentation for eCRFs

- Adverse event reports and any supporting documentation
- Investigational plan deviations
- Complete medical records relative to the study

10.12 Investigator Reports

As stated in Section 8.1.5, the investigator is required to report cannulation procedure and/or device-related AEs to the EDC system and UADEs to the reviewing IRB within ten working days of discovery. The investigator is also required to follow any other applicable IRB reporting requirements. The investigator is required to notify the sponsor of withdrawal of IRB approval with five working days and to submit annual study progress reports to the IRB and sponsor. An investigator shall notify the sponsor and IRB of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency. Such notice shall be given as soon as possible, but not later than five working days after the emergency occurred. An investigator will report the use of Veinplicity without prior subject informed consent to the sponsor and IRB with five working days after the use occurs.

10.13 Investigational Site Termination

The sponsor may terminate an investigational site for any of the following reasons:

- Failure to secure subject informed consent or HIPAA authorization prior to enrollment
- Failure to properly report adverse events, according to regulatory and/or IRB requirements
- Repeated investigational plan violations
- Failure to enroll an adequate number of subjects
- Loss of or unaccounted for study product inventory
- Administrative decision by the company

10.14 Sponsor Records

The sponsor (or RCRI) will maintain the following records:

- Investigational plan and all amendments.
- Signed Clinical Trial Agreements.
- Institutional Review Board approval letters, including a copy of the approved consent form(s).
- All correspondence relating to this study between the Sponsor, RCRI and the investigational site, IRB and FDA.
- CVs for all study personnel.
- Site personnel signatures and responsibility lists.
- Investigational device inventory log including: date, quantity, and lot numbers of devices shipped to and returned by the sites.

10.15 Sponsor Reports

- UADE evaluations to FDA, IRB and investigators – 10 working days of notice.
- Withdrawal of IRB approval to FDA, other IRB and investigators – 5 working days.
- Withdrawal of FDA approval to IRB and investigators – 5 working days.
- Failure to obtain informed consent to FDA - 5 working days of notice.

10.16 Investigational Plan Amendments

Investigators may not modify this investigational plan. The sponsor may amend this investigational plan during the study, and such amendments will be submitted to the IRBs by the sites for approval.

10.17 Investigational Plan Deviations

Any deviations from this investigational plan undertaken to protect the life or physical well-being of a subject in an emergency situation must be reported to RCRI within five working days of occurrence, and the respective IRB as soon as possible but in no event later than five working days after the emergency occurs. All investigational plan deviations must be reported to the EDC system on the Protocol Deviation eCRF.

11. References

1. Hallam C et al. Development of the UK Vessel Health and Preservation (VHP) framework: a multi-organizational collaborative. *J Infect Prev*. 2016;17:65-72.
2. Infusion Nurses Society. *Policies and Procedures for Infusion Therapy.* 5th ed. Short Term Peripheral Catheter Placement. Tizra Publishing;2016:pp 53-8. Available at: http://ins.tizrapublisher.com/hha7v4/76. Accessed 29 May 2018.
3. Mehta CR, Pocock SJ. Adaptive increase in sample size when interim results are promising: a practical guide with examples. *Stat Med.* 2011;30(28):3267-84. doi: 10.1002/sim.4102. Epub 2010 Nov 30.
4. Aponte H et al. The use of ultrasound for placement of intravenous catheters. *AANA Journal.* 2007;7^5: 212-6.
5. Riker M et al. Validation and refinement of the difficult intravenous access score: a clinical prediction rule for identifying children with difficult intravenous access. *Acad Emerg Med.* 2011;18:1129–34.
6. Sabri A et al. Failed attempts and improvement strategies in peripheral intravenous catheterization. *Biomed Mater Eng.* 2013;23:93–108.
7. Houghton PE, Nussbaum EL and Hoens AM. Electrophysical agents. *Physiother Can.* 2010;62:1-83. DOI:10.3138/ptc.621.5.

EXHIBIT 3

Regulatory & Clinical Research Institute, Inc.
5353 Wayzata Blvd., Suite 505
Minneapolis, MN 55416-1334
Tel: 952-746-8080
Fax: 952-884-6518
Project Title: Integrated Solution for Regulatory, Health Economics and Clinical Trial Support for the Veinplicity Device

WORK ORDER FORM

This Work Order is considered an addendum to a mutually-executed Master Services Agreement and describes the scope of services to be performed. Please review, sign and date this form, and return to RCRI via mail, fax or email a scanned copy to your RCRI contact and initiate payment for any required retainer. Work on the project cannot begin until both the signed work order and retainer are received. Thank you for working with RCRI.

Project Title: Integrated Solution for Regulatory, Health Economics & Clinical Trial Support for the Veinplicity Device	
Contact Name: Patrick Kullmann, CEO	**Work Order Date:** 26 March 2018
Company Name: Physeon GmbH Herrenacker 15, 8200 Schaffhausen, Switzerland	**Office Phone #:** (866) 243-8111 **Mobile Phone #:** (763) 516-1029 **Email:** patrick.kullmann@physeon.com
RCRI Contact Name: Peggy Pereda, MS, VP Clinical Sciences [(952) 715-3107; ppereda@rcri-inc.com]	**Executed NDA:** ☒ Yes **Retainer Required:** ☐ No ☒ Yes
☒ **New Work Order; Code:**	**RCRI Project Code:**

Description of Work:

RCRI will provide Regulatory, Health Economics and Clinical Trial consulting support to Physeon GmbH for the Veinplicity Device as detailed in the Preliminary Project Estimate titled *"Integrated Solution for Regulatory, Reimbursement, and Clinical Trial Support for the Veinplicity Device"* Version 2, dated 19 March 2018.

Will a Business Associate relationship exist between the client and RCRI? ☒ No ☐ Yes

Significant Deliverables/Milestones/Other Project Specifications:	**Estimated Timeline:**
1. Prepare FDA Pre-Submission 2. Prepare for and participate in Pre-Sub Teleconference 3. Provide IDE Template and Review IDE Submission 4. Analyze Available Clinical Data 5. Consult on Adding Economic Data to Clinical Trial Data 6. Develop an Interactive Excel Model / Sales Tool 7. OPTIONAL: Add Facility-Specific Look-up Feature to Excel Model 8. Provide support for the Veinplicity Clinical Study	TBD

Estimate: $397,244 – $409,224 *[$343,322 – $355,302 consulting fees; $53,922 pass through costs]*

REGULATORY SUPPORT: $20,590 – $27,910

1. FDA Pre-Submission Preparation [20 – 30 hours Regulatory Sr. Principal Advisor] ..... $6,600 – $9,900
2. Pre-Sub Teleconference and Preparation [10 – 14 hours Regulatory Sr. Principal Advisor] ..... $3,190 – $4,510
3. Provide Template and Review IDE Submission [40 - 50 hours Blended hourly rate of $270] ..... $10,800 – $13,500

HEALTH ECONOMICS SUPPORT: $11,750 – $16,410

Prior to Clinical Study:

1. Analyze Available Clinical Data ..... $3,070 – $4,270
2. Consult on Adding Economic Data to Clinical Trial Data ..... $1,200 – $2,400

After Completion of Clinical Study:

3. Develop an Interactive Excel Model / Sales Tool
   a. Develop structure of economic model ..... $3,740 – $5,470
   b. Enter Data into Model and Add Customizability Features ..... $3,740 – $4,270
4. OPTIONAL: Add Facility-Specific Look-up Feature to Excel Model ($6,000 – $7,200; not included in estimate above)

Regulatory & Clinical Research Institute, Inc.
5353 Wayzata Blvd., Suite 505
Minneapolis, MN 55416-1334
Tel: 952-746-8080
Fax: 952-884-6518
Project Title: Integrated Solution for Regulatory, Health Economics and Clinical Trial Support for the Veinplicity Device

CLINIAL TRIAL SUPPORT: $364,904 *[$310,982 consulting fees; $53,922 pass through costs]*

Consulting Tasks	*Multi-center*
A. Study Initiation	*$30,875*
B. Site Activation	*$32,135*
C. Site Management and Monitoring	*$56,509*
D. Data Management	*$66,423*
F. Data Analysis	*$59,900*
G. Clinical Reports	*$31,800*
H. Project Management and Communication	*$33,340*
Consulting TOTAL	***$310,982***

Pass Through Costs	*Multi-center Assumptions*	*Estimate*
Regulatory Binder Supplies	*$50 per binder; 5 binders*	*$250*
*Travel Costs for Site Qualification Visit(s)**	*MN site*: $50 per 1-day visit; 1 onsite visit* *non-MN sites**: $1,450 per 1-day visit; 3 onsite visits*	*$4,400*
*Travel Costs for Site Initiation Visit(s)**	*MN site*: $50 per 1-day visit; 1 onsite visit* *non-MN sites**: $1,450 per 1-day visit; 2 onsite visits*	*$2,950*
*Travel Costs for Interim Monitoring Visits**	*MN site*: $100 per 2-day visit; 1 onsite visit* *non-MN sites**: $1,900 per 2-day visit; 2 onsite visits*	*$3,900*
*Travel Costs for Close-out Monitoring Visits**	*MN site*: $100 per 2-day visit; 1 onsite visit* *non-MN sites**: $1,900 per 2-day visit; 2 onsite visits*	*$3,900*
Database Hosting/Usage, Help Desk, Support	*3 sites; 400 subjects; 10 eCRFs per subject; 40,000 total datapoints; randomization module; 4 months*	*$38,222*
Phone Calls/Photocopies/Shipping Costs	*$50 per month; 6 months project duration*	*$300*
Pass-Through TOTAL		***$53,922***

** Travel cost assumptions for MN site based on: $25 per day food and $25 per day parking.*
*** Travel cost assumptions for non-MN sites based on: $1,000 travel; $200 per night lodging; $100 per day food; $100 per day ground transportation; and $50 per day parking.*

Estimates are provided for client budgeting purposes. Actual time for work performed will be billed, which may be more or less than the estimate provided here.

☐ **Estimate not provided**

Retainer $30,000

Company agrees that upon completion of the above deliverables (unless modified by a subsequent work order), RCRI has fulfilled its obligation under this Work Order. The specifications outlined are based on the project requirements and assumptions set forth herein. Any changes to the project requirements or assumptions may require a new work order. Cost estimates are based on current billing rates. Company and Consultant shall agree in writing to any changes to the project specifications prior to any work being started on such changes. RCRI work orders are valid for a period of 60 days from work order date.

Consultant and Company agree to this Work Order. Company hereby authorizes commencement of the Services.

Client Signature:	**Date:** 28 Mar 2018
Client Printed Name: Brucé Kunsman	
RCRI Signature:	**Date:** 26MAR2018
RCRI Printed Name: Peggy J. Pereda	

		Pre-Study			Start-Up		Execution		Close-out		
		Apr '18	May '18	Jun '18	Jul '18	Aug '18	Sep '18	Oct '18	Nov '18	Dec '18	Total
Regulatory Support											
1. FDA Pre-Sub Preparation	$9,900	$9,900	-	-	-	-	-	-	-	-	$0
2. Pre-Sub Teleconference and Preparation	$4,510	-	$4,510	-	-	-	-	-	-	-	$0
3. IDE Template and Submission Review	$13,500	-	-	$13,500	-	-	-	-	-	-	$0
Subtotal	$27,910	$9,900	$4,510	$13,500	$0	$0	$0	$0	$0	$0	$27,910
Health Economic Support											
1. Analyze Available Data	$4,270	$4,270	-	-	-	-	-	-	-	-	$0
2. Advise on Economic Data to Collect in Study	$2,400	-	$1,200	$1,200	-	-	-	-	-	-	$0
3. Develop Interactive Excel Model	$9,740	-	-	-	-	-	-	-	-	$9,740	$9,740
Subtotal	$16,410	$4,270	$1,200	$1,200	$0	$0	$0	$0	$0	$9,740	$16,410
Clinical Study Support											
A. Study Initiation Tasks											
1. Project Start-up and Team Training	$7,265	$2,480	-	-	$4,785	-	-	-	-	-	$4,785
2. Clinical Protocol	$16,500	$4,125	$4,125	$4,125	$4,125	-	-	-	-	-	$16,500
3. ICF Template	$1,600	-	-	-	-	$1,600	-	-	-	-	$1,600
4. NDA Template	$420	-	-	-	-	$420	-	-	-	-	$420
5. Budget & CTA Template	$2,240	-	-	-	$2,240	-	-	-	-	-	$2,240
6. Site Training Materials	$2,850	-	-	-	-	$2,850	-	-	-	-	$2,850
Subtotal	$30,875	$6,605	$4,125	$4,125	$11,150	$4,870	$0	$0	$0	$0	$30,875
B. Site Activation Tasks											
1. Investigational Site ID	$2,100	-	-	-	$2,100	-	-	-	-	-	$2,100
2. NDA Negotiation	$1,680	-	-	-	$1,680	-	-	-	-	-	$1,680
3. Investigational Site Qualification	$8,935	-	-	-	$1,560	$7,375	-	-	-	-	$8,935
4. Investigational Site Selection	$275	-	-	-	-	$275	-	-	-	-	$275
5. Budget and CTA Negotiation	$6,720	-	-	-	-	$2,240	$4,480	-	-	-	$6,720
6. ICF Negotiation	$1,325	-	-	-	-	-	$1,325	-	-	-	$1,325
7. Site Set-up Support	$10,050	-	-	-	-	-	$10,050	-	-	-	$10,050
8. Reg Binder Assembly & Distribution	$1,050	-	-	-	-	-	$1,050	-	-	-	$1,050
Subtotal	$32,135	$0	$0	$0	$5,340	$9,890	$16,905	$0	$0	$0	$32,135

		Pre-Study			Start-Up		Execution		Close-out		
		Apr '18	May '18	Jun '18	Jul '18	Aug '18	Sep '18	Oct '18	Nov '18	Dec '18	Total
C. Site Management and Monitoring Tasks											
1. Monitoring Plan and Training	$5,963	-	-	-	-	$5,963	-	-	-	-	$5,963
2. Site Initiation Visits	$8,973	-	-	-	-	$1,170	$7,803	-	-	-	$8,973
3. Interim Monitoring Visits	$18,333	-	-	-	-	-	$6,111	$12,222	-	-	$18,333
4. Study Close-Out Visits	$19,503	-	-	-	-	-	-	-	$6,500	$13,003	$19,503
5. Site Management & Communication	$1,350	-	-	-	$225	$225	$225	$225	$225	$225	$1,350
6. Site Payments	$2,388	-	-	-	-	-	$263	-	$1,600	$525	$2,388
Subtotal	**$56,509**	**$0**	**$0**	**$0**	**$225**	**$7,358**	**$14,402**	**$12,447**	**$8,325**	**$13,753**	**$56,509**
D. Data Management Tasks											
1. CRF Content	$6,310	-	-	-	$6,310	-	-	-	-	-	$6,310
2. Edit Check Specs	$3,895	-	-	-	$3,895	-	-	-	-	-	$3,895
3. DB Dev & Val	$20,405	-	-	-	-	$20,405	-	-	-	-	$20,405
4. User Acceptance Testing	$4,050	-	-	-	-	$4,050	-	-	-	-	$4,050
5. EDC Training Materials	$1,640	-	-	-	-	$1,640	-	-	-	-	$1,640
6. EDC Training Sessions	$860	-	-	-	-	-	$860	-	-	-	$860
7. DB Lock, Transfer, Archive	$430	-	-	-	-	-	-	-	$215	$215	$430
8. Client Communication re: DB	$430	-	-	-	$215	$215	-	-	-	-	$430
9. Data Management Plan & Training	$3,308	-	-	-	-	$2,975	$333	-	-	-	$3,308
10. Ongoing Data Review & Query Management	$25,095	-	-	-	-	-	$10,085	$7,505	$7,505	-	$25,095
Subtotal	**$66,423**	**$0**	**$0**	**$0**	**$10,420**	**$29,285**	**$11,278**	**$7,505**	**$7,720**	**$215**	**$66,423**
F. Data Analysis Tasks											
1. Sample Size Calculation	*	-	-	-	-	-	-	-	-	-	$0
2. Randomization Schedule	$4,675	-	-	-	-	$4,675	-	-	-	-	$4,675
3. SAP	$6,600	-	-	-	-	-	$6,600	-	-	-	$6,600
4. Statistical Report Shell	$6,600	-	-	-	-	-	$6,600	-	-	-	$6,600
5. Statistical Code Development & Validation	$27,100	-	-	-	-	-	$13,550	$13,550	-	-	$27,100
6. Interim Analysis & Validation	$2,710	-	-	-	-	-	-	$2,710	-	-	$2,710
7. Final Analysis & Validation	$10,840	-	-	-	-	-	-	-	$10,840	-	$10,840
8. Client Communication re: Data Analysis	$1,375	-	-	-	-	-	$344	$344	$344	$344	$1,375
Subtotal	**$59,900**	**$0**	**$0**	**$0**	**$0**	**$4,675**	**$27,094**	**$16,604**	**$11,184**	**$344**	**$59,900**
G. Clinical Report Tasks											
1. Final Report	$30,700	-	-	-	-	-	-	-	$23,100	$7,600	$30,700
2. Client Communication re: Final Report	$1,100	-	-	-	-	-	-	-	$550	$550	$1,100
Subtotal	**$31,800**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$23,650**	**$8,150**	**$31,800**

		Pre-Study			Start-Up		Execution		Close-out		
		Apr '18	May '18	Jun '18	Jul '18	Aug '18	Sep '18	Oct '18	Nov '18	Dec '18	Total
H. Project Management & Communication Tasks											
1. Project Team Meetings with Client	$6,870	-	-	-	$1,145	$1,145	$1,145	$1,145	$1,145	$1,145	$6,870
2. Project Mgmt and Client Communication	$19,800	-	-	-	$3,300	$3,300	$3,300	$3,300	$3,300	$3,300	$19,800
3. RCRI Internal Team Meetings	$4,170	-	-	-	$695	$695	$695	$695	$695	$695	$4,170
4. Project Files Transfer and Archive	$2,500	-	-	-	-	-	-	-	-	$2,500	$2,500
Subtotal	$33,340	$0	$0	$0	$5,140	$5,140	$5,140	$5,140	$5,140	$7,640	$33,340
Clinical Consulting Estimate Total	$310,982	$6,605	$4,125	$4,125	$32,275	$61,218	$74,819	$41,696	$56,019	$30,102	$310,982
Pass Through Costs											
Regulatory Binder Supplies	$250	-	-	-	$250						$250
Travel Costs for Site Qualification Visits**	$4,400	-	-	-		$4,400					$4,400
Travel Costs for Site Initiation Visits**	$2,950	-	-	-			$2,950				$2,950
Travel Costs for Interim Monitoring Visits**	$3,900	-	-	-			$1,300	$2,600			$3,900
Travel Costs for Close-out Monitoring Visits**	$3,900	-	-	-					$1,300	$2,600	$3,900
Database Hosting/Usage, Support	$38,222	-	-	-			$9,556	$9,556	$9,556	$9,556	$38,222
Long Distance Phone Calls/Shipping/Printing/...	$300	-	-	-	$50	$50	$50	$50	$50	$50	$300
Clinical Study Pass-Through Estimate Total	$53,922	$0	$0	$0	$300	$4,450	$13,856	$12,206	$10,906	$12,206	$53,922
Clinical Study Grand Total	$364,904	$6,605	$4,125	$4,125	$32,575	$65,668	$88,674	$53,901	$66,924	$42,307	$364,904
Integrated Project Grand Total	$409,224	$20,775	$9,835	$18,825	$32,575	$65,668	$88,674	$53,901	$66,924	$42,307	$409,224

** not included in original estimate; work will be done under protocol development; an inordinate number of scenarios may necessitate an increase in the budgeted amount.*

*** travel cost assumptions based on: $1,000 travel; $200 per night lodging; $100 per day food; $100 per day ground transportation; and $50 per day parking for non-MN sites and: $25 per day food and $25 per day parking for MN sit.*